AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (original): A purified and isolated AMIGO nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising the amino acid sequence shown in SEQ ID NO:2, 4 or 6.

Claim 2 (original): A purified and isolated nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:1, 3 or 5.

Claim 3 (original): A purified and isolated nucleic acid comprising a recombinant nucleotide sequence comprising a nucleotide sequence shown in SEQ ID NO:1, 3 or 5 or a homolog or fragment thereof.

Claim 4 (original): An expression construct comprising the nucleic acid according to claim 2 operatively linked to an expression control sequence, said expression construct capable of encoding an AMIGO polypeptide or variants thereof.

Claim 5 (original): A host cell transformed or transfected with the expression construct of claim 4.

Claim 6 (original): A host cell transformed or transfected

with a polynucleotide wherein said polynucleotide includes a strand containing a human nucleotide sequence that hybridizes to a DNA comprising the non-coding strand complementary to SEQ ID NO:1, 3 or 5, under the following hybridization conditions:

(a) hybridization at 42 °C for 20 hours in a solution containing 50% formamide, 5 X SSPE, 5 X Denhardt's solution, 0.1% SDS and 0.1 mg/ml denatured salmon sperm DNA; and

(b) washing the filter twice for thirty minutes at room temperature and twice for thirty minutes at 65 °C with a wash solution containing 1xSSC, and 0.1% SDS.

Claim 7 (original): An isolated and purified AMIGO polypeptide comprising the amino acid sequence of SEQ ID NO:2, 4 or 6.

Claim 8 (original): Method of producing an AMIGO polypeptide according to claim 7, said method comprising the steps of:
culturing a host cell of claim 5 comprising a polynucleotide encoding said polypeptide operably associated with a promoter sequence such that the nucleic acid sequence
encoding said polypeptide is expressed; and
isolating said polypeptide from said host cell or from a growth medium in which said host cell is cultured.

Claim 9 (original): Method of producing antibodies comprising:
- immunising a mammal with the isolated and purified AMIGO protein of claim 7 or an antigenic fragment thereof.

Claim 10 (original): Use of the isolated and purified AMIGO protein of claim 7 or an antigenic fragment thereof as an antigen.

Claim 11 (original): An antibody produced by the method of claim 9.

Claim 12 (original): The antibody of claim 11 which is labeled with a detectable label.

Claim 13 (original): A kit of reagents for use in detecting the presence of AMIGO or allelic variant thereof in a biological sample, comprising

- a container; and in said container:
- a compound, preferably labeled, capable of detecting AMIGO or allelic variants thereof.

Claim 14 (original): The kit according to claim 13, wherein said compound is a primer or probe.

Claim 15 (original): The kit according to claim 13, wherein said compound is an antibody as defined in claim 11.

Claim 16 (Currently Amended): The kit according to ~~any one claims 13-14~~ claim 13 for assessing the predisposition of an individual to a condition mediated by variation or dysfunction of AMIGO.

Claim 17 (original): The kit according to claim 16 further comprising instructions for using the kit.

Claim 18 (original): A transgenic non-human animal containing a human or murine AMIGO gene as a transgene.

Claim 19 (original): A transgenic non-human animal containing a transgene or insertion disrupting expression of an AMIGO gene or a homolog thereof.

Claim 20 (original): A pharmaceutical compound comprising AMIGO nucleic acid molecule, AMIGO protein, AMIGO peptide fragment, AMIGO fusion protein, AMIGO agonists, AMIGO antagonists or anti-AMIGO antibody.

Claim 21 (original): Method for treatment of a condition dependent on AMIGO wherein a pharmaceutically effective amount of the compound of claim 20 is administered to a patient in need of such treatment.

Claim 22 (original): Method for affinity purification of ligand that binds to the AMIGO comprising the following steps: a) contacting a source of AMIGO receptor with an immobilized AMIGO under conditions whereby the AMIGO receptor to be purified is selectively adsorbed onto the immobilized AMIGO; (b) washing the immobilized AMIGO and its support to remove non-adsorbed material; and (c) eluting the AMIGO receptor molecules from the immobilized AMIGO to which they are adsorbed with an elution buffer.

Claim 23 (original): A method for identifying a modulator of binding between an AMIGO receptor and an AMIGO receptor, comprising steps of:

(a) contacting an AMIGO receptor composition with an AMIGO composition in the presence and in the absence of a putative

modulator compound;

(b) detecting binding between AMIGO receptor and the AMIGO receptor in the presence and absence of the putative modulator; and

(c) identifying a modulator compound in view of decreased or increased binding between the AMIGO receptor and the AMIGO receptor in the presence of the putative modulator, as compared to binding in the absence of the putative modulator.

Claim 24 (original): A method according to claim 23, further comprising a step of:

(d) making a modulator composition by formulating a modulator identified according to step (c) in a pharmaceutically acceptable carrier.

Claim 25 (original): A method according to claim 24, further comprising a step of:

(e) administering the modulator composition to an animal that comprises cells that express the AMIGO receptor, and determining physiological effects of the modulator composition in the animal.

Claim 26 (Currently Amended): A method according to ~~any one of claims 23-25,~~ claim 23, wherein the AMIGO receptor composition comprises a member selected from the group consisting of:

(a) a purified polypeptide comprising a AMIGO receptor extracellular domain fragment that binds the AMIGO;

(b) a phospholipid membrane containing AMIGO receptor polypeptides; and

(c) a cell recombinantly modified to express increased amounts of an AMIGO receptor on its surface.

Claim 27 (Currently Amended): A method according to ~~any one of claims 23-25,~~ claim 23, wherein the AMIGO receptor composition comprises an AMIGO receptor extracellular domain fragment bound to a solid support.

Claim 28 (Currently Amended): A method according to ~~any one of claims 23-25,~~ claim 23, wherein the AMIGO receptor composition comprises an AMIGO receptor extracellular domain fragment fused to an immunoglobulin Fc fragment.

Claim 29 (Currently Amended): A method according to ~~any one of claims 23-25,~~ claim 23, wherein the AMIGO receptor is selected from the group consisting of a mammalian AMIGO, AMIGO2, and AMIGO3.

Claim 30 (currently amended): A method according to ~~any one of claims 23-29~~ claim 23, wherein the AMIGO receptor is human.

Claim 31 (currently amended): A method according to ~~any one of claims 23-30~~ claim 23, wherein the AMIGO composition comprises a member selected from the group consisting of:

(a) a purified polypeptide comprising an AMIGO fragment that binds the AMIGO receptor;

(b) a phospholipid membrane containing AMIGO polypeptides; and

(c) a cell recombinantly modified to express increased amounts of an AMIGO on its surface.

Claim 32 (currently amended): A method according to ~~any one of 23-30~~ claim 23, wherein the AMIGO composition comprises an AMIGO extracellular domain fragment bound to a solid support.

Claim 33 (currently amended): A method according to ~~any one of claims 23-30~~ claim 23, wherein the AMIGO composition comprises an AMIGO extracellular domain fragment fused to an immunoglobulin Fc fragment.

Claim 34 (currently amended): A method according to ~~any one of claims 23-33~~ claim 23, wherein the AMIGO is human.

Claim 35 (currently amended): A method according to ~~any one~~

~~of claims 23-25~~ claim 23, wherein the AMIGO receptor composition comprises a cell recombinantly modified to express increased amounts of an AMIGO receptor on its surface, and wherein the detecting step comprises measuring an AMIGO binding-induced physiological change in the cell.

Claim 36 (currently amended): A method according to ~~any one of claims 23-25~~ claim 23, wherein the AMIGO composition comprises a cell recombinantly modified to express increased amounts of an AMIGO on its surface, and wherein the detecting step comprises measuring an AMIGO binding-induced physiological change in the cell.

Claim 37 (original): A method for screening for selectivity of a modulator of binding between an AMIGO and an EGFR, comprising steps of:

a) contacting an AMIGO receptor composition with an EGFR composition in the presence and in the absence of a compound that modulates binding between the AMIGO receptor and EGFR receptor; and

b) detecting binding between the AMIGO receptor composition and the EGFR receptor composition in the presence and absence of the modulator compound,

c) identifying the selectivity of the modulator compound in view of decreased or increased binding between the AMIGO receptor and

the EGFR receptor in the presence as compared to the absence of the modulator, wherein increased selectivity of the modulator for modulating AMIGO EGFR binding correlates with decreased differences in AMIGO- EGFR binding.

Claim 38 (original): A method of modulating growth, migration, axonal growth, myelination, fasciculation or proliferation of cells in a mammalian organism, comprising a step of:

(a) identifying a mammalian organism having cells that express a AMIGO receptor and/or EGFR; and

(b) administering to said mammalian organism a composition, said composition comprising an agent selected from the group consisting of:

(i) a polypeptide comprising an AMIGO receptor that binds to the AMIGO receptor and/or EGFR, or a nucleic acid encoding said polypeptide;

(ii) a polypeptide comprising a fragment of the AMIGO, wherein the polypeptide and fragment retain AMIGO binding characteristics of the AMIGO, or a nucleic acid encoding said polypeptide;

(iii) an antibody that specifically binds the polypeptide of (i) or (ii) in a manner that inhibits the polypeptide from binding the AMIGO receptor and/or EGFR, or a fragment of the antibody that specifically binds the polypeptide of (i) or (ii);

(iv) a polypeptide comprising an antigen-binding fragment of

(iii) and that inhibits the polypeptide of (i) or (ii) from binding the AMIGO receptor and/or EGFR;
(v) a molecule that selectively inhibits AMIGO binding to the AMIGO receptor without inhibiting AMIGO binding to the EGFR receptor; and
(vi) a molecule selectively binding to the AMIGO receptor and the EGFR receptor;

wherein the composition is administered in an amount effective to modulate growth, migration, or proliferation of cells that express AMIGO in the mammalian organism.

Claim 39 (original): A method according to claim 38, wherein the mammalian organism is human.

Claim 40 (Currently Amended): A method according to claim 38 ~~or 39~~, wherein the cells comprise neuronal cells.

Claim 41 (currently amended): A method according to ~~any one of claims 38-40~~ claim 38, wherein the organism has a disease characterized by aberrant growth, migration, or proliferation of neuronal cells/neuronal extensions.

Claim 42 (currently amended): A method according to ~~to any one of claims 38-41~~ claim 38, wherein the conditions comprises a neuronal trauma.

Claim 43 (original): A method according to claim 38, further comprising administering a second agent to the patient for modulating neuronal growth, migration, regeneration or proliferation, said second agent selected from the group consisting of: an antibody that specifically binds with any of the foregoing polypeptides, an antibody that specifically binds with a receptor for any of the foregoing polypeptides, or a polypeptide comprising an antigen binding fragment of such antibodies.

Claim 44 (original): A method according to claim 38, wherein the AMIGO extracellular fragment is conjugated with Fc domain.

Claim 45 (original): A method according to claim 44, wherein rat AMIGO Fc fusion protein sequences have been replaced essentially with the human AMIGO and Fc sequences

Claim 46 (currently amended): A polypeptide according to ~~claims 38-45~~ claim 38, for use in the manufacture of a medicament for the treatment of diseases characterized by aberrant growth, migration, regeneration or proliferation of cells that express an AMIGO receptor.

Claim 47 (currently amended): Method according to ~~claims 38-45~~ claim 38 wherein neuronal cells are selected from the group consisting of: hippocampal cells, cerebral cells, cerebellar cells, neuronal trauma cells, glial scar cells, spinal cord cells, optic nerve cells, retina cells, kidney cells, and cells acting during fasciculation, guidance, growth, or myelination.

Claim 48 (original): A method of modulating cancer, tumour growth or metastasis in a mammalian organism, comprising a step of:

(a) identifying a mammalian organism having cells that express an AMIGO receptor and/or EGFR; and

(b) administering to said mammalian organism a composition, said composition comprising an agent selected from the group consisting of:

(i) a polypeptide comprising an AMIGO receptor that binds to the AMIGO receptor and/or EGFR, or a nucleic acid encoding said polypeptide;

(ii) a polypeptide comprising a fragment of the AMIGO, wherein the polypeptide and fragment retain AMIGO binding characteristics of the AMIGO, or a nucleic acid encoding said polypeptide;

(iii) an antibody that specifically binds the polypeptide of (i) or (ii) in a manner that inhibits the polypeptide from binding the AMIGO receptor and/or EGFR, or a fragment of the antibody that specifically binds the polypeptide of (i) or (ii);

(iv) a polypeptide comprising an antigen-binding fragment the (iii) and that inhibits the polypeptide of (i) or (ii) from binding the AMIGO receptor and/or EGFR;
(v) a molecule that selectively inhibits AMIGO binding to the AMIGO receptor without inhibiting AMIGO binding to the EGFR receptor; and
(vi) a molecule selectively binding to the AMIGO receptor and the EGFR receptor;
wherein the composition is administered in an amount effective to modulate cancer growth or metastasis of cells that express AMIGO in the mammalian organism.

Claim 49 (original): A method according to claim 48, wherein the mammalian organism is human.

Claim 50 (original): A method according to claim 48 ~~or 49~~, wherein the cells comprise glioma, glioblastoma, astrocytoma, anaplastic astrocytoma, ependymomas, oligodendrogliomas, medulloblastomas, meningiomas, schwannomas, craniopharyngiomas, germ cell tumors, pineoblastoma, pineocytoma, germinoma cells, lung carcinoma, breast carcinoma, ovarian carcinoma, colorectal carcinoma, bladder carcinoma, pancreatic carcinoma, squamous cell carcinoma, or renal carcinoma cells.

Claim 51 (currently amended): A method according to ~~any one of claims 48-50~~ claim 48, wherein the organism has a disease

characterized by cancer or metastasis.

Claim 52 (original): A method according to claim 51, wherein the condition comprises a brain tumor.

Claim 53 (original): A method according to claim 48, further comprising administering a second agent to the patient for modulating cancer growth or metastatic growth of cancer, said second agent selected from the group consisting of: an antibody that specifically binds with any of the foregoing polypeptides, an antibody that specifically binds with a receptor for any of the foregoing polypeptides, or a polypeptide comprising an antigen binding fragment of such antibodies.

Claim 54 (original): A method according to claim 48, wherein the AMIGO extracellular fragment is conjugated with Fc domain.

Claim 55 (original): A method according to claim 48, wherein rat AMIGO Fc fusion protein sequences have been replaced essentially with the human AMIGO and Fc sequences

Claim 56 (original): Method for treatment of cancer or metastatic growth of cancer cells selected from the group consisting of: glioma, glioblastoma, astrocytoma, anaplastic

astrocytoma, ependymomas, oligodendrogliomas, medulloblastomas, meningiomas, schwannomas, craniopharyngiomas, germ cell tumors of germinoma cells, lung carcinoma, breast carcinoma, ovarian carcinoma, colorectal carcinoma, bladder carcinoma, pancreatic carcinoma, squamous cell carcinoma, and renal carcinoma, comprising a step of administering to a subject in need of such treatment the compound as claimed in claim 20.

Claim 57 (original): Method for treatment of neuronal cells selected from the group consisting of: hippocampal cells, cerebral cells, cerebellar cells, neuronal trauma cells, glial scar cells, spinal cord cells, optic nerve cells, retina cells, kidney cells, and cells acting during fasciculation, guidance, growth, or myelination, comprising a step of administering to a subject in need of such treatment the compound as claimed in claim 20.

Claim 58 (original): A polypeptide or a nucleic acid encoding said polypeptide, said polypeptide comprising a fragment of an AMIGO that binds to an AMIGO receptor, for use in the manufacture of a medicament for the treatment of diseases characterized by aberrant growth, migration, regeneration or proliferation of cells that express an AMIGO receptor.

Claim 59 (original): A method of modulating the phosphorylation of a human epidermal growth factor receptor in

cells or tissues comprising contacting said cells or tissues with the AMIGO compounds.

Claim 60 (original): The method of claim 59, wherein said AMIGO compounds comprises AMIGO peptides encoded a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5.

Claim 61 (original): The method of claim 59, wherein said AMIGO compounds comprise an anti-AMIGO antibody.